

In re Application of :  
U.S. Serial No.:  
For:

Jagath L. KADURUGAMUWA *et al.*  
09/370,860

**NOVEL VACCINES AND PHARMACEUTICAL COMPOSITIONS  
USING MEMBRANE VESICLES OF MICROORGANISMS, AND  
METHODS FOR PREPARING SAME**



**EXHIBIT 1**

**"MARKED UP" AMENDMENTS TO CLAIMS PURSUANT TO RULE 1.121(c)**

1. (Amended) A cellular vaccine against an infectious disease caused by an infectious agent comprising a bacterial carrier strain having a membrane vesicle of a microorganism integrated into the cell surface of the carrier strain, wherein the membrane vesicle comprises a bilayer and has an amount of an antigen associated with its surface, which antigen is produced by the microorganism from which the membrane vesicle is derived [which is effective to provide protection against the infectious agent].

6. (Amended) A vaccine as claimed in claim 1 which is effective against another infectious agent comprising a second bacterial carrier strain having a membrane vesicle of a microorganism integrated into the cell surface of the second carrier strain, wherein the membrane vesicle comprises a bilayer and has an amount of an antigen associated with its surface, which antigen is produced by the microorganism from which the membrane vesicle is derived [which is effective to provide protection against the infectious agent].

18. A vaccine as claimed in claim 1 wherein the bacterial carrier strain is selected from the group consisting of *Shigella*, *Salmonella*, *Vibrio*, and *Escherichia*.

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19. A vaccine as claimed in claim 18 wherein the bacterial carrier strain is *S. typhi* Ty21a or *S. typhimurium*.

20. A vaccine as claimed in claim 3 wherein the microorganism is selected from the group consisting of *Pseudomonas aeruginosa*, *Shigella flexneri*, *Shigella dysenteriae*, *Escherichia coli*, *Salmonella typhi*, *Neisseria gonorrhoeae* and combinations thereof.

21. A cellular vaccine comprising an avirulent or attenuated bacterial carrier strain having a membrane vesicle integrated into a cell wall of the carrier strain, the membrane vesicle having a bilayer and being derived from a pathogenic bacteria, wherein integration of the membrane vesicle with the cell wall of the carrier strain provides antigenic factors produced by the pathogenic bacteria to a surface of the bacterial carrier strain.

22. A method of producing a cellular vaccine according to claim 21 comprising:

- (a) incubating an avirulent or attenuated bacterial carrier strain with a membrane vesicle derived from a pathogenic bacteria;
- (b) selecting a carrier strain having a membrane vesicle integrated into its cell wall; and

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- (c) forming a vaccine with the carrier strain of step (b).